

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
21 July 2005 (21.07.2005)

PCT

(10) International Publication Number
WO 2005/066180 A1

(51) International Patent Classification⁷: **C07D 491/04,**
A61K 31/407

(21) International Application Number:
PCT/GB2005/050003

(22) International Filing Date: 6 January 2005 (06.01.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0400022-0 8 January 2004 (08.01.2004) SE
0401332-2 26 May 2004 (26.05.2004) SE

(71) Applicant (for all designated States except US): **MEDIVIR AB** [SE/SE]; Lunastigen 7, S-141 44 Huddinge (SE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **NILSSON, Magnus** [SE/SE]; Medivir AB, Lunastigen 7, S-141 44 Huddinge (SE). **ZHOU, Xiao-Xiong** [SE/SE]; Medivir AB, Lunastigen 7, S-141 44 Huddinge (SE). **ODEN, Lourdes** [PH/SE]; Medivir AB, Lunastigen 7, S-141 44 Huddinge (SE). **CLASSON, Bjorn** [SE/SE]; Medivir AB, Lunastigen 7, S-141 44 Huddinge (SE). **NOREN, Rolf** [SE/SE]; Medivir AB, Lunastigen 7, S-141 44 Huddinge (SE). **GRABOWSKA, Urszula** [GB/GB]; Medivir UK Ltd, Chesterford Research Park, Little Chesterford, Essex CM10 1XL (GB). **JACKSON, Phillip** [GB/GB]; Medivir UK Ltd, Chesterford Research Park, Little Chesterford, Essex CM10 1XL (GB). **FALLON, Phillip** [GB/GB]; Medivir UK Ltd, Chesterford Research Park, Little Chesterford, Essex CM10 1XL (GB). **CARR, Andrew** [GB/GB]; Medivir UK Ltd, Chesterford Research Park,

Little Chesterford, Essex CM10 1XL (GB). **LILEY, Mark** [GB/GB]; Medivir UK Ltd, Chesterford Research Park, Little Chesterford, Essex CM10 1XL (GB). **TOZER, Matt** [GB/GB]; Medivir UK Ltd, Chesterford Research Park, Little Chesterford, Essex CM10 1XL (GB). **JOHNSON, Tony** [GB/GB]; Medivir UK Ltd, Chesterford Research Park, Little Chesterford, Essex CM10 1XL (GB). **DIAZ, Victor** [ES/GB]; Medivir UK Ltd, Chesterford Research Park, Little Chesterford, Essex CM10 1XL (GB). **CRESPO, Lala** [ES/GB]; Medivir UK Ltd, Chesterford Research Park, Little Chesterford, Essex CM10 1XL (GB). **KANGASMETSÄ, Jussi** [SE/GB]; Medivir UK Ltd, Chesterford Research Park, Little Chesterford, Essex CB11 1XL (GB). **BONNAUD, Thierry** [FR/GB]; Medivir UK Ltd, Chesterford Research Park, Little Chesterford, Essex CB11 1XL (GB).

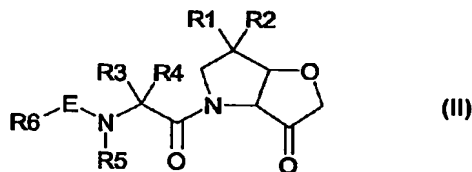
(74) Agents: **TEUTEN, Andrew, J. et al.**; Sagittarius Intellectual Property Consultants Ltd, Taylor House, 39 High Street, Marlow, Bucks SL7 1AF (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,

[Continued on next page]

(54) Title: CYSTEINE PROTEASE INHIBITORS



(57) Abstract: A compound of the formula (II) wherein one of R¹ and R² is halo and the other is H or halo; R³ is C₁-C₄ straight or branched chain, optionally fluorinated, alkyl; R⁴ is H; or R³ together with R⁴ and the adjoining backbone carbon defines: a spiro-C₃-C₇ cycloalkyl, optionally substituted with 1 to 3 substituents selected from halo, hydroxyl, C₁-C₄ alkyl or C₁-C₄ haloalkyl; or optionally bridged with a methylene group; or a C₄-C₆ saturated heterocycle having a hetero atom selected from O, NRa, S, S(=O)₂; where Ra is H, C₁-C₄ alkyl or CH₃C(=O); R⁵ is independently selected from H or methyl; E is -C(=O)-, -S(=O)_m-, -NR⁵S(=O)_m-, -NR⁵C(=O)-, -OC(=O)-, R⁶ is a stable, optionally substituted, monocyclic or bicyclic, carbocyclic or heterocyclic; m is independently 0, 1 or 2; are inhibitors of cathepsin K and useful in the treatment or prophylaxis of osteoporosis.



FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG).

— *before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments*

Published:

— *with international search report*

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*